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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,794	08/21/2001	Melvyn Little	31304-756.831	5254

21971 7590 09/21/2005

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EXAMINER	
TUNGATURTHI, PARITHOSH K	
ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/674,794	LITTLE ET AL.	
	Examiner	Art Unit	
	Parithosh K. Tungaturthi	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *August 2nd, 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *12-19 and 22-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *06.28.05; 08.21.01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-11 and 20-21, in the reply of August 1st, 2005 is acknowledged.

2. Claims 12-19, 22-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions. Applicant timely traversed the restriction (election) requirement in the reply on August 1st, 2005.

3. Claims 1-11 and 20-21 are under examination.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim1-11, 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a multivalent Fv antibody construct having atleast four variable domains wherein two variable regions are light chain variable regions and two are heavy chain variable regions, does not reasonably provide enablement for a multivalent Fv antibody construct having any other combination of the number of heavy and/or light chain variable regions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

a. Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

b. The claims are broadly drawn to a multivalent antibody construct having atleast four variable domains which can be interpreted as an antibody construct with a combination of any number of heavy or light chain or completely consisting of four heavy chains or heavy light chains.

c. The specification teaches a multivalent Fv antibody construct having at least four variable domains which are linker with each other via linker 1, 2 ad 3, wherein two variable regions are selected from heavy chain variable regions and the other two are selected from light chain variable regions (figure 1, in particular). The specification fails to enable a multivalent Fv antibody construct wherein all four variable regions are selected from "heavy chain" or "all from light chain variable regions" or "3 light chain and 1 heavy chain" or "3 heavy chain and 1 light chain variable".

d. The claims are not commensurate in scope with the enablement provided in the specification. It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which

provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function.

e. It is unlikely that antibodies as defined by the claims, which may contain "all heavy chain" or "all light chain" variable regions or "an unequal number of heavy and light chain variable regions", have the required binding function. The specification provides no direction or guidance regarding how to produce all antibodies as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

One of skill in the art would neither expect not predict the appropriate functioning of the antibody as broadly as is claimed.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 1-11 and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mezes et al (U.S. Patent 5,892,020; Filed: June 7th, 1995) in view of Hollinger et al (U.S. Patent 5837242; Filed December 3rd, 1993) and Pastan et al (U.S. Patent 5,635,599; Issued June 3rd, 1997) and Whitlow et al (U.S. Patent 5,856,456; Filed April 7th, 1994) and Coloma and Morrison (Nature Biotechnology 1997 Vol. 15:15-163; IDS – 08.21.05).

The instant claims are drawn to a multivalent F_v antibody construct at least four variable domains, wherein said variable domains are linked with one another via a peptide linker 1, a peptide liner 2 and a peptide linker 3. wherein said peptide linker 1

and said peptide linker 3 have about 1 to about 10 amino acids, wherein said F_v antibody construct is bivalent, wherein said peptide linker 2 has about 11 to about 20 amino acids, wherein said peptide linker 2 has about 3 to about 10 amino acids, wherein said F_v antibody construct is multispecific, is bispecific, is monospecific, and a composition comprising the multivalent F_v antibody construct for diagnosis and/or treatment of a disease, wherein said disease is a viral, a bacterial or a tumoral disease. In addition, the claims are drawn to a multivalent F_v antibody wherein said peptide linker 1 and peptide linker 3 have the amino acid sequence GG, wherein said peptide linker 2 has the amino acid sequence $(G_4S)_4$, wherein said Fv antibody construct is tetravalent, and further wherein said peptide linker 2 comprises the amino acid sequence GGPGS.

Mezes et al teach multivalent single chain antibodies which have two or more biologically active antigen binding sites (see abstract, in particular). The multivalent single chain antibodies are formed by using a peptide linker to covalently link two or more single chain antibodies, each single chain antibody having a variable light domain linked to a variable heavy chain domain by a peptide linker. The antibody fragments can be joined to form bivalent single chain antibodies having the order of V_l and V_h domains as follows: V_l-L-V_h-L-V_l-L-V_h; V_l-L-V_h-L-V_h-L-V_l; V_h-L-V_l-L-V_h-L-V_l; V_h-L-V_l-L-V_l-L-V_h; in addition to V_h-L-V_h-L-V_l-L-V_l; V_l-L-V_l-L-V_h-L-V_h. Single chain multivalent antibodies which are trivalent and greater have one or more antibody fragments joined to a bivalent single chain antibody by an additional interpeptide linker (column 3, in particular). Mezes also teach that the single chain antibody fragments can be derived

from the light and/or heavy chain variable domains of any antibody. Preferably, the light and heavy chain variable domains are specific for the same antigen. The individual antibody fragments which are joined to form a multivalent single chain antibody may be directed against the same antigen or can be directed against different antigens (column 4 lines 1-8, in particular). Mezes et al also teach that to form the antibody fragments and multivalent single chain antibodies, it is necessary to have a suitable peptide linker. Suitable linkers for joining the V_h and V_l domains are those which allow the V_h and V_l domains to fold into a single polypeptide chain which will have a three dimensional structure very similar to the original structure of a whole antibody from which antibody fragment is derived. Suitable linkers for linking the scFvs are those which allow the linking of two or more scFvs such that the V_h and V_l domains of each immunoglobulin fragment have a three dimensional structure such that each fragment maintains the binding specificity of the whole antibody from which the immunoglobulin fragment is derived (columns 5 lines 1-13, in particular). The linker is generally about 10 to about 50 amino acid residues (column 5 lines 36-41, in particular). Mezes et al also teaches a noncovalently linked Fv single chain antibody (Fv2) (figure 1-3, in particular), specifically a CC49 Fv2 wherein two CC49 scFv non-covalently linked such that V_l of one scFv2 interacts with V_h of an other scFv2 to form a dimer as shown in figure 1-3 (column 7 lines 58-61, in particular). Mezes et al also teach that the multivalent single chain antibodies provide unique benefits for use in diagnostics and therapeutics, and that the use of multivalent single chain antibodies afford a number of advantages over the use of larger fragments or entire antibody molecules by reaching their target tissue

more rapidly, and are cleaved quickly from the body (column 6 last paragraph, in particular). Mezes et al also teach that for diagnostic and/or therapeutic uses, the multivalent single chain antibodies can be constructed such that one or more antibody fragments are directed against a diagnostic or therapeutic agent, in addition to a pharmaceutical compositions which are particularly advantageous for use in the diagnosis and/or therapy of disease, such as cancer (column 7 lines 1-10, in particular).

Mezes et al does not specifically teach that the linkers joining the variable domains, peptide linker 1 and peptide linker 3, have the amino acid sequence GG, or wherein said peptide linker 2 comprises the amino acid sequence $(G_4S)_4$ or GGPGS. Further Mezes et al does not teach that the Fv antibody construct is tetravalent. These deficiencies are made up for by Hollinger et al, Pastan et al, Whitlow et al and Coloma and Morrison.

Hollinger et al teach polypeptides comprising a first domain, which comprises a binding region of an immunoglobulin heavy chain variable region, and second domain, which comprises a binding region of an immunoglobulin light chain variable region, the domains being linked but incapable of associating with each other to form an antigen binding site, associate to form antigen binding multimers, such a dimers, associate to form multivalent or have multipsecificity (see abstract in particular). Hollinger et al teach that the domains of the polypeptide are linked by a peptide linker, the linker may be "short", consisting of a too few amino acids to allow the VL domain of a chain to combine with the VH domain of that chain. This may be less than 10 amino acids, most preferably, 5, 4, 3, 2, or 1. It may be in certain cases that 9, 8, 7 or 6 amino acids are

suitable (column 3 lines 45-51, in particular). Hollinger et al teach an embodiment wherein the heavy and light chain variable domains are connected by a linker that does not allow pairing between the two domains on the same, e.g. because it is too short, and the domains are therefore forced to pair with the complementary domains of another chain and create two antigen binding sites, further explained that short linkers impose major constraints on the ways by which two chains can associate (column 15 lines 10-30, in particular). Hollinger et al furthermore teach that VH-VL polypeptides linked by a 15 amino acid linker are able to pair their VH and VL domains both as monomers and as dimmers in the diabody format, VH-VL polypeptides with a 5-amino acid linker are only able to pair their VH and VL domain by forming dimers in the diabody format (column 16 lines 48-54, in particular). Hollinger et al also suggested that one should choose antibodies for which the VH and VL domains are known to associate and form a stable FV fragment in analogy to the diabody design using short linkers (5 residues) to prevent the VH and VL domains on the same chain from pairing with each other (column 20 lines 8-14, in particular). Hollinger et al also teach the construction of a diabody using "two glycine residues" as a linker (column 53 line 25-40, in particular).

Pastan et al teach novel modified forms of ligands wherein the amino and carboxy ends are joined through a linker (column 1 lines 60-67, in particular) for example SEQ ID NO:55 comprising $(G_4S)_4$, wherein the ligands refer generally to all molecules capable of reacting with or otherwise recognizing or binding to a receptor on a target cell and specific examples of ligands include, but are not limited to antibodies (column 4 lines 19-23, in particular) wherein the term antibody includes various forms of

modified or altered antibodies, such as an intact immunoglobulin, an v fragment containing only the light and heavy chain variable regions, an Fv fragment linked by a disulfide bond, an Fab or (Fab)'2 fragment containing the variable regions and parts of the constant regions, a single chain antibody and the like (columns 4 and 5, definition of "antibody" in particular).

Whitlow et al (U.S. Patent 5,856,456) teach that a novel peptide linker comprising the amino acid sequence from about 2 to about 20 having a first end connected to a first protein domain, and having a second end connected to a second protein domain, wherein the peptide comprises at least one proline residue within the sequence, the proline being position next to a charged amino acid, and the charged amino acid-proline pair is positioned within the peptide linker to inhibit proteolysis of said polypeptide. (column 4 lines 33-44, in particular). Whitlow et al also teach a novel peptide linker comprising the amino acid sequence: U_mXPZ_n wherein U and Z can be single amino acids, such that n and m are any integers from 0 to 48 and n+m is not greater that 48, and X is a charged amino acid.

Coloma and Morrison teach the production of two different versions of a bispecific antibody using a novel technique that includes joining a single chain antibody after the (ScFv) after the hinge or C terminus of a heavy chain constant region, and that the ligation of the ScFv downstream of the hinge or the constant region through a five amino acid mini-linker, rich in serines and glycines, provides flexibility to the ScFv possibility facilitating its binding to antigen (pages 160-161, First paragraph of discussion in particular). Coloma and Morrison et al also teach that bispecific

antibodies provide potential tools for use in immunotherapy by taking advantage of the great specificity of variable regions for their antigens and can be envisioned as transporters of therapeutic drugs or molecules or even immune effector cells to the specific targets identified by one of their binding sites. Following this novel strategy for the production of bispecific antibodies it is possible to generate molecules recognizing a wide variety of antigen combinations. Other possibilities suggested by the success of this approach include a multivalent antibody with different specificities in each ScFv, tetravalent antibodies with increased avidity as well as molecules with tandem ScFvs providing additional binding sites at the carboxy terminus of the antibody or even at the amino terminus of the heavy or light chain. (page 162, last paragraph of discussion in particular).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have generated a multivalent F_v antibody construct at least four variable domains, wherein said variable domains are linked with one another via a peptide linker 1, a peptide linker 2 and a peptide linker 3, wherein non-covalently linked Fv single chain antibody (Fv2) can be formed wherein two scFv non-covalently linked such that V_l of one scFv2 interacts with V_h of an other scFv2 to form a dimer, wherein said F_v antibody construct is bivalent and can be multispecific, bispecific or monospecific and a composition comprising the multivalent F_v antibody construct for diagnosis and/or treatment of a disease, wherein said disease is a viral, a bacterial or a tumoral disease as taught by Mezes et al; wherein the said peptide linkers

1 and 3 have the amino acid sequence GG as taught by as taught by Hollinger et al, wherein said peptide linker 2 has the amino acid sequence $(G_4S)_4$ as taught by Pastan et al or the amino acid sequence GGPGS as taught by Whitlow et al, and further wherein the Fv antibody construct is tetravalent as taught by Coloma and Morrison.

One of ordinary skill in the art would have been motivated and would have reasonable expectation of success to have generated a multivalent F_v antibody construct at least four variable domains, wherein said variable domains are linked with one another via a peptide linker 1, a peptide linker 2 and a peptide linker 3, as taught by Mezes et al and vary the length of the linkers as taught by Hollinger et al because Mezes et al teach multivalent single chain antibodies formed by using a peptide linker to covalently link two or more single chain antibodies, each single chain antibody having a variable light domain linked to a variable heavy chain domain by a peptide linker and that the linker is generally about 10 to about 50 amino acid residues, in addition to a noncovalently linked Fv single chain antibody (Fv2) (figure 1-3), specifically a CC49 Fv2 wherein two CC49 scFv non-covalently linked such that V_l of one scFv2 interacts with V_h of an other scFv2 to form a dimer as shown in figure 1-3, and because Hollinger et al teach polypeptides comprising a V_h and V_l linked by a linker that does not allow pairing between two domains of the same polypeptide and renders V_h and V_l of the same chain incapable of associating with each other to form an antigen binding site, and the domains are therefore forced to pair with the complementary domains of another chain

and create two antigen binding sites, to form antigen binding multimers, such as dimers, associate to form multivalent or have multipsecificity.

In addition, one of ordinary skill in the art would have been motivated and would have had a reasonable expectation of success to have generated a multivalent F_v antibody construct wherein said F_v, antibody construct, wherein the antigen binding site may be formed by the non-covalent interaction of V_h and V_l of the same scFv or a different scFv molecule(s) and hence can be bivalent and multispecific, bispecific or monospecific and a composition comprising the multivalent F_v antibody construct for diagnosis and/or treatment of a disease, wherein said disease is a viral, a bacterial or a tumoral disease a taught by Mezes et al and introduce short peptide sequences for linkers 1 and 3, for example GG, for the formation of a bivalent antibody as disclosed in figure 1B because Hollinger et al teach polypeptides comprising a first domain, which comprises a binding region of an immunoglobulin heavy chain variable region, and second domain, which comprises a binding region of an immunoglobulin light chain variable region, the domains being linked but incapable of associating with each other to form an antigen binding site, associate to form antigen binding multimers, such a dimers, associate to form multivalent or have multipsecificity, wherein the domains of the polypeptide are linked by a peptide linker, the linker may be "short", consisting of a too few amino acids to allow the VL domain of a chain to combine with the VH domain of that chain (less than 10 amino acids), in addition to the construction of a diabody using "two glycine residues" as a linker.

Moreover, one of ordinary skill in the art would have known to introduce the amino acid sequence GGPGS for a linker as taught by Whitlow et al because Whitlow et al teach a novel peptide linker comprising the amino acid sequence from about 2 to about 20 and further because Whitlow et al teach a novel peptide linker comprising the amino acid sequence: U_mXPZ_n wherein U and Z can be single amino acids, such that n and m are any integers from 0 to 48 and n+m is not greater that 48, and X is a charged amino acid.

Further, one of ordinary skill in the art would have known to generate a multivalent F_v antibody construct as taught by Mezes et al and Hollinger et al wherein said peptide linker 2 has the amino acid sequence $(G_4S)_4$ as taught by Pastan et al because Pastan et al teach novel modified forms of ligands wherein the amino and carboxy ends are joined through a linker for example SEQ ID NO:55 comprising $(G_4S)_4$, wherein the ligands refer generally to all molecules capable of reacting with or otherwise recognizing or binding to a receptor on a target cell and specific examples of ligands include, but are not limited to antibodies.

Furthermore, one of ordinary skill in the art would have been motivated and would have had a reasonable expectation of success to have generated a multivalent F_v antibody construct at least four variable domains, wherein said variable domains are linked with one another via a peptide linker 1, a peptide linker 2 and a peptide linker 3. as taught by Mezes et al and introduce the amino acid sequence "GG" for linkers 1 and 3 as taught by Hollinger et al and " $(G_4S)_4$" as linker 2 as taught by Pastan et al to yield a multivalent F_v antibody as disclosed in figure 1B **OR** "GGPGS" as linker 2 as taught by

Whitlow et al to yield a multivalent F_v antibody as disclosed in figure 1C because Hollinger et al teach an embodiment wherein the heavy and light chain variable domains are connected by a linker that does not allow pairing between the two domains on the same, e.g. because it is too short, and the domains are therefore forced to pair with the complementary domains of another chain and create two antigen binding sites.

Thus, it would have been obvious to one skilled in the art to combine the multivalent antibody, wherein a non-covalent linkage can be formed between the V_h and V_l of two different scFv chains such that V_l of one scFv2 interacts with V_h of an other scFv2, and/or vice versa to form a dimer as taught by Mezes et al and utilize the linkers "GG" for linkers 1 and 3 as taught by Hollinger et al, and " $(G_4S)_4$" or "GGPGS" for linkers 2 as taught by Pastan et al and Whitlow et al, respectively, because Hollinger et al suggested that one should choose antibodies for which the VH and VL domains are known to associate and form a stable FV fragment in analogy to the diabody design using short linkers (5 residues) to prevent the VH and VL domains on the same chain from pairing with each other, further explained that short linkers impose major constraints on the ways by which two chains can associate and because Hollinger et al furthermore teach that VH-VL polypeptides linked by a 15 amino acid linker are able to pair their VH and VL domains both as monomers and as dimers in the diabody format, VH-VL polypeptides with a 5-amino acid linker are only able to pair their VH and VL domain by forming dimers in the diabody format

Hence, it would have been obvious to one skilled in the art to have generated a multivalent F_v antibody construct at least four variable domains, wherein said variable

domains are linked with one another via a peptide linker 1, a peptide linker 2 and a peptide linker 3, with varying lengths of peptide linkers, wherein said F_v antibody construct is bivalent and can be multispecific, bispecific or monospecific and a composition comprising the multivalent F_v antibody construct for diagnosis and/or treatment of a disease, wherein said disease is a viral, a bacterial or a tumoral disease as taught by Mezes et al wherein said Fv antibody construct is tetravalent as taught by Coloma and Morrison, wherein the said peptide linker 1 and said peptide linker 3 have the amino acid sequence GG as taught by Hollinger et al and wherein said peptide linker 2 has the amino acid sequence GGPGS as taught by Whitlow et al or $(G_4S)_4$ as taught by Pastan et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

9. No claims are allowed

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

11. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
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Ph: (571) 272-8789

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER